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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,845	12/20/2001	Thomas Backenfeld	PLOVIN-5	1446

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 10/022,845	Applicant(s) BACKENFELD ET AL.	
	Examiner Patrick T. Lewis	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *35 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34 and 37-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Europe on December 20, 2000. It is noted, however, that applicant has not filed a certified copy of the 00610134.9 application as required by 35 U.S.C. 119(b).

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-13 and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, and 6 of U.S. Patent No. 5,798,338 ('338). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-13 and 22 differ from the '338 patent in that the composition of the '338 patent is not limited to a granulate preparation having a humidity of at most 60%;

however, the '338 patent teaches that the complexes are optionally processed into the desired dosage forms, such as tablets, powder, granulates, etc. (column 2, lines 44-49). The '338 patent further teaches that the complex is dried in a vacuum with phosphorous pentoxide (column 3, lines 8-11).

Claim Objections

4. Claims 10-13 are objected to because of the following informalities: the terms "of polyvinylpyrrolidone of polyvinylpyrrolidone" is unclear. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 8, 9, 26-27, and 37-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 8 and 9, applicant has failed to particularly point out the modifications to said compounds which distinctly set forth the structural core modifications or chemical moieties effectuating said derivatization. In the absence of distinct modifications or derivatizing moieties, the term "derivatives" is indefinite in all occurrences.

Claim 26 contains two (2) periods. Since a claim is limited to a single sentence, it is unclear whether the limitation(s) following the first period are part of the claimed invention.

In claim 27, the phrase "wherein the estrogen is in an amount correspondent to a therapeutically equivalent amount of ethinyl estradiol" renders the claim indefinite as it is unclear what amount of estrogen is present in the composition.

Regarding claims 37-46, the term "granulation conditions" has not been described in such a way as to apprise one of ordinary skill in the art of the parameters under which the granulation process occurs. In the absence of clear recitation of active methodological steps, it is impossible for the skilled artisan to practice the instantly claimed invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Backensfeld et al. U.S. Patent 5,798,338 (Backenfeld) in combination with Parikh et al. U.S. Patent 6,228,399 (Parikh), Pitha U.S. Patent 4,596,795 (Pitha), Krattenmacher *Contraception* (**2000**), vol. *62*, pages 29-38 (Krattenmacher)

Claim 1 is drawn to a formulation comprising a complex between an estrogen and a cyclodextrin, wherein the formulation is a granulate preparation having a relative humidity of at most 60%, as determined at a temperature between 20 °C and 40 °C. Claims 1-24 depend from claim 1 with claims 2-5, 8, 10-14, and 20-22 depending directly from claim 1. Claims 2-5 further limit the relative humidity of the formulations. Claims 6-7 limit the estrogen. Claims 8-9 limit the cyclodextrin. Claims 10-13 limit the concentration of polyvinylpyrrolidone present in the formulation. Claims 14-19 limit additional therapeutic agents present in the formulation. Claim 20 is limited to micronized formulations. Claim 21 limits the formulations by requiring an antioxidant.

Claims 22-24 limit ratio of estrogen and cyclodextrin present in the formulation. Claim 25 is drawn to a composition comprising an estrogen and a cyclodextrin and one or more excipients, the composition having a stability such that said estrogen is in an amount of at least 85% w/w in relation to the initial content of said estrogen after storage for 12 months at a temperature between 40 °C and 75% relative humidity. Claims 26-34 depend from claim 25. Claim 26 limits the relative humidity of the formulation. Claims 27-29 limit the amount of estrogen in the formulation. Claims 30-31 limit the amount of estrogen and the cyclodextrin. Claims 32-34 require drospirenone as part of the composition.

Backensfeld teaches compositions comprising an inclusion complex of ethinyl estradiol and β-cyclodextrin (column 1, lines 27-46; column 3, lines 16-27; claim 6). The complex can be processed into the desired dosage forms, such as tablets, poweder, granulates, etc. after the addition of the commonly used additives, such as, lactose, starch, polyvinylpyrrolidone, magnesium stearate, and preservatives (column 2, lines 44-49). Backenfeld teaches the ratio of cyclodextrin to sex hormone in the complex as 1:1, 2:1, 3:1, 3:2 or 1:2 (column 2, lines 50-61). Backenfeld further teaches that the complex is dried in a vacuum with phosphorous pentoxide (column 3, lines 5-11).

Backensfeld differs from the instantly claimed invention in that Backensfeld does not teach: 1) the relative humidity of the composition, 2) compositions comprising one or more additional active agents, 3) micronized formulations, nor 4) long-term stability of the complex. However, these deficiencies are taught by the prior art and would have been obvious to one of ordinary skill in the art at the time of the invention.

Pitha teaches the administration of a combination of sex hormones, particularly testosterone, progesterone and estradiol in the form of their inclusion complexes with a cyclodextrin as an oral contraceptive and for the treatment of premenstrual tension syndrome (FIG 1; column 3 lines 39-44; column 1, lines 52-57; FIG. 3-4; column 4, lines 1-25).

Krattenmacher teaches that drospirenone is a progestogen having a pharmacological profile closely related to progesterone, especially with regard to antimineralocorticoid and antiandrogenic activities (page 29, column 2, second paragraph). Krattenmacher also teaches that adverse effects related to other oral contraceptives may be decreased using drospirenone and that contraceptive efficacy and adverse effects of drospirenone/ethinyl estradiol combination treatment have been evaluated with favorable results.

Parikh teaches that microparticles (particles having diameters of from nanometers to micrometers) provide some specific advantages over the unformulated non-micronized drug particles (column 1, lines 32-47). The advantages include improved oral bioavailability of drugs that are poorly absorbed from GI tract, development of injectable formulations that are currently available only in oral dosage form, less toxic injectable formulations that are currently prepared with organic solvents, sustained release of intramuscular injectable drugs that are currently administered through daily injection or constant infusion, and preparation of inhaled, ophthalmic formulation of drugs that otherwise could not be formulated for nasal or ocular use.

It would have been obvious to one of ordinary skill in the art at the time of the invention to produce a composition/formulation comprising a complex between an estrogen and a cyclodextrin as instantly claimed in view of the prior art. Although Backesnfeld is silent on the relative humidity of the composition/formulation, it does teach drying the complex under vacuum with phosphorous pentoxide. One of ordinary skill in the art would expect the composition, when dried, to have a relative humidity less than 40%. It would have also been obvious to one of ordinary skill to complex a combination of an estrogen and a progestogen as Pitha teaches such. Although Pitha does not teach drospirenone, it would have been obvious to substitute drospirenone for progesterone in the inclusion complex as Krattenmacher teaches that drospirenone is a progestogen having a pharmacological profile closely related to progesterone, especially with regard to antimineralocorticoid and antiandrogenic activities. The skilled artisan would expect a reasonable degree of success in substituting one member of a group for another since both members have similar therapeutic activity. The combination of varying ratios of drospirenone and cyclodextrin is seen to be within the purview of the skilled artisan.

In regards to the long-term stability of the composition/formulation, Backensfeld teaches drying the complex and applicant states on page 15 of the instant disclosure that the relative humidity of the composition/formulation is the most important factor relating to stability. Thus, the dried composition/formulation is seen to meet the stability limitations of the instantly claimed invention. Since the Office does not have the facilities for preparing the claimed materials and comparing when with prior art

inventions, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. One of ordinary skill in the art at the time of the invention would be motivated to make said modifications in order to reduce the steroidal dosages used. This in turn would lead to a reduction in side effects

Conclusion

11. Claims 1-46 are pending. Claims 1-34 and 37-46 are rejected. Claims 35-36 are drawn to a nonelected invention. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 8:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patrick T. Lewis
Examiner
Art Unit 1623

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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June 27, 2003